BC Environment

A REVIEW OF THE ENVIRONMENTAL IMPACT AND TOXIC EFFECTS OF IPBC

N.D. Henderson
Prepared for:
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SUMMARY

The purpose of this paper is to review the environmental fate and toxic effects of 3-iodo-2-propynyl butyl carbamate (IPBC). IPBC is found in one antisapstain formulation, NP-1, currently used as a replacement for chlorophenols in the lumber industry.

Laboratory studies indicate that IPBC undergoes rapid hydrolysis at pH 9, but is stable at pH 5. It is moderately adsorbed by several soil types, and is expected to have a moderate potential for movement in the soil environment. The compound is rapidly degraded under aerobic soil conditions; microbial metabolism seems to be the most important factor accounting for its degradation.

IPBC is quickly absorbed from the intestinal tract in rats, and is rapidly metabolised or excreted via the kidney and lung. Small amounts are retained in the carcasses of rats after 10 days. Tests on laboratory animals showed that the chemical is moderately toxic via oral and dermal routes, is severely irritating to the eyes, is only slightly irritating to the skin, and is not a sensitizer. It is moderately toxic to extremely toxic to two fish species, with a 96 hour LC50 of 0.067 ppm for rainbow trout.

Tests indicate that IPBC is not carcinogenic, mutagenic, or teratogenic. Occupational exposure should be minimal, provided proper protective equipment and procedures are employed.

TABLE OF CONTENTS

		PAGE
Summary		2
Table of Contents		3-4
1.0	INTRODUCTION	5
2.0	HISTORICAL BACKGROUND AND USES	5
3.0	PHYSICAL AND CHEMICAL PROPERTIES	6
4.0	ENVIRONMENTAL IMPACT	6-8
	4.1 Environmental Sources	6
	4.2 Environmental Distribution	6
	4.3 Environmental Behaviour	7
	4.3.1 Aqueous Hydrolysis	7
	4.3.2 Adsorption/Desorption	7
	4.3.3 Aerobic Soil Metabolism	8
5.0	PHARMACOKINETICS	9-10
	5.1 Absorption, Transport, and Distribution	9
	5.2 Metabolism and Excretion	9-10
	5.3 Placental and Milk Transfer	10
6.0	TOXICOLOGICAL EFFECTS	10-13
	6.1 Mammalian Toxicity	10-11
	6.2 Aquatic Toxicity	11-12
	6.2.1 Bioconcentration	12
	6.3 Avian Toxicity	12
	6.4 Comparative Toxicity	13

		PAGE
7.0	CARCINOGENICITY	13
8.0	MUTAGENICITY	13-14
9.0	TERATOGENICITY AND REPRODUCTIVE EFFECTS	14-15
10.0	IMPACTS OF OCCUPATIONAL EXPOSURE	15-16
11.0	ANALYTICAL METHODS OF DETECTION	16
12.0	EXISTING LEGISLATION	17
13.0	CONCLUSION	17
14.0	REFERENCES	18-24
Table 1 -	A comparison of toxicity values of antisapstain chemicals	25
APPENDIX A -	Databases Searched for Information on IPBC	26
APPENDIX B -	Mammalian Lethal Toxicity Classes for Chemical Compounds	27
APPENDIX C -	Aquatic Lethal Toxicity Classes for Chemical Compounds	28
APPENDIX D -	Calculation of an Acceptable Daily Intake (ADI) of IPBC for Humans	29
APPENDIX E -	Derivation of Stormwater Effluent Criteria for IPBC	30
APPENDIX F -	Calculation of an Air Emission Guideline for IPBC	31-32

1.0 INTRODUCTION

Large volumes of chlorophenol compounds have previously been used in Canada to preserve and protect wood from attack by various pests. Concerns about acute aquatic toxicity, occupational impacts, and presence of hazardous impurities, including dioxins and furans, in chlorophenols are among the reasons for dissatisfaction with their use (1). The Canadian Lumber Industry thus phased out the use of chlorinated phenols for sapstain control after Agriculture Canada deregistered the antisapstain use of chlorophenols in 1990 (78). The use of alternative chemicals has therefore increased.

Acceptable antisapstain chemicals should pose a minimal hazard to human and environmental health while adequately protecting lumber from sapstain and decay mould and fungi (2). Currently there are several chemicals registered with Agriculture Canada which may be used for the protection of freshly cut lumber, including 2-(thiocyanomethylthio)benzo-thiazole (TCMTB), 3-iodo-2-propynyl butyl carbamate (IPBC), didecyldimethylammonium chloride (DDAC), sodium carbonate, sodium borate, azaconazole, and copper-8-quinolinolate (Cu-8).

The purpose of this paper is to review and evaluate the available information concerning the physical and chemical properties, environmental sources and distribution, toxicity, and pharmacokinetics of IPBC. The compound is used in one antisapstain product, NP-1, which has recently been reviewed by BC Environment, Lands, and Parks (4). Appendix A contains a list of the computerized databases searched for citations on IPBC. Information was also provided by the manufacturer, Troy Chemical Corporation of Newark, New Jersey.

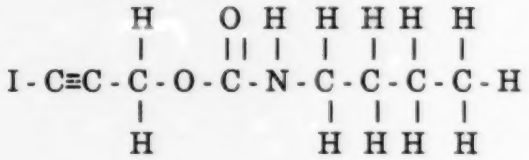
2.0 HISTORICAL BACKGROUND

IPBC was registered as an antimicrobial with the United States Environmental Protection Agency in 1978 by Troy Chemical Corporation (12), and a request for registration in Canada followed in 1980. Temporary registration of IPBC, effective September 1, 1990 and subject to annual review, was granted in Canada in July 1990 (61).

The technical product, marketed as Troysan Polyphase P100, is under patent with Troy until January 23, 1996. It is widely used as a consumer and industrial mildewcide in paints and adhesives, as an antimicrobial in metalworking fluids and on canvas and cordage, and as a chemical in wood treatment. Ninety-five percent of extensive US sawmill treatment reportedly involves IPBC (11). A 40% IPBC solution is used in the production of the antisapstain product NP-1 (12), but IPBC constitutes only 7.6% of the marketed product.

3.0 PHYSICAL AND CHEMICAL PROPERTIES

The chemical structure of IPBC is shown below.



(CAS No. 55406-53-6)

It is a white crystalline powder with a specific odour, a high solubility in aromatic solvents such as acetone and benzyl alcohol (16), and a moderate solubility in water (about 156 mg/L at 20-30°C) (30). It is chemically stable at 54°C (7), and melts at about 66°C (28). The specific gravity is 1.575 (16), and the vapour pressure is 0.002 Pa. The octanol/water partition coefficient (Kow) for IPBC has been measured at 646 (log Kow = 2.81) (6).

The technical product is minimum 97% pure, with primary impurities of sodium chloride (0.9% maximum) and tri-iodo-allyl butyl carbamate (<0.1%) (28). The Material Safety Data Sheet for the product used in the preparation of NP-1 specifies a mixture of 40% IPBC, 25% naphthalene, 17.5% dipropylene glycol, and 17.5% dimethyl sulfoxide (30). The chemical does not contain dioxins, and formation of dioxins is apparently unlikely (11).

IPBC reportedly decomposes during incineration (temperature unspecified) to form carbon monoxide, carbon dioxide, nitrogen dioxide, dinitrogen oxide, and hydrogen iodide (11). Incineration studies were not available for review.

4.0 ENVIRONMENTAL IMPACT

4.1 Environmental Sources

IPBC is likely not a naturally occurring substance. Sources in the environment could include spills and other accidental discharges, permitted discharges from commercial facilities using or manufacturing the chemical, and discharges from products treated with IPBC, including wood and paints.

4.2 Environmental Distribution

No studies on ambient environmental levels were located. However, the manufacturer has stated that following a spill, the chemical will not be detectable in the environment after 28 days (Detection Limit, DL = 25 ppm) (30).

4.3 Environmental Behaviour

Three studies on hydrolysis, adsorption/desorption, and aerobic soil metabolism have been received from the manufacturer. These are reviewed below, with other available studies. An anaerobic soil metabolism study is presently underway, and a leaching study is also being considered by the manufacturer (12).

4.3.1 Aqueous Hydrolysis

Initial hydrolysis studies (10) found that, in the absence of microbes and/or nutrients, IPBC solutions were hydrolytically stable, although data were not provided. The aqueous hydrolysis of 99.6% pure IPBC (Troysan Polyphase P-100) in buffered solutions of pH 5, 7, and 9 at 25°C has been investigated (62). Initial IPBC concentrations were 151.3 ug/L. The compound was degraded very rapidly in pH 9 buffered solution, with a half-life of less than one day. The only metabolite detected was propargyl butyl carbamate (PBC). At pH 7, degradation was much slower, with a half-life of 139 days. At pH 5, IPBC was hydrolytically stable; degradation was not observed.

4.3.2 Adsorption/Desorption

IPBC is predicted to be minimally adsorbed by soil, and is expected to have a moderate potential for soil movement (3). One study reports that the chemical has an affinity for organics and does not tend to be mobile (11). The manufacturer has provided one study on IPBC behaviour in soil which found a moderate potential for movement; it is summarized below.

Troysan Polyphase P-100 (P-100) adsorption/desorption by soils was investigated using radioisotope techniques (63) via the batch equilibrium (slurry) method (65). Initial P-100 concentrations of approximately 100, 50, 10, and 1 ug/mL and a solution:soil ratio of 5:1 were used in five soil types: a Hanford sandy loam, a Centhan sand, a Blackoar loam, a Mexico silty clay, and an Evesboro sand. The study was performed at 22°C, and all samples were exposed to laboratory fluorescent lighting. Three desorption steps were performed on those soils receiving the highest initial P-100 concentration.

P-100 was adsorbed in moderate amounts by the soils used in this study, with adsorption Koc values ranging from 61.0 to 309. Results show that the P-100 adsorption did not appear to be directly related to either soil organic matter content, clay content, or cation exchange capacity. P-100 was readily degraded to PBC in suspensions from the Evesboro, Blackoar, and Mexico soils. Differences in relative adsorption between soils may have been related to differences in the extent of IPBC degradation.

4.3.3 Aerobic Soil Metabolism

Carbamate compounds similar to IPBC may persist in soil for weeks or months (5), and microbial metabolism seems to be the most important factor accounting for their degradation (8). One study of biotransformation involved incubation of soil containing IPBC for various periods of time (10). After incubation from 0 to 12 days, samples were filter sterilized to remove naturally occurring bacteria (unspecified), then either analyzed for remaining IPBC or incubated for a further period of time and then analyzed.

Results indicate that IPBC degradation does take place with the aid of microorganisms present in the soil, and is relatively rapid compared to degradation of other carbamates (75). Addition of substrates which stimulate microbial growth increased the rate of degradation, providing further evidence that the process is bacteriological. However, the presence of ammonium salts (NH_4-) and organic amendments in the soil seemed to have a slight inhibitory effect on microbial action. All products of the degradation reactions were said to be biodegradable, but these products were not specified. The proposed metabolic pathway involves an initial decarbamylation reaction, followed by reductive and/or oxidative reactions.

A progress report from the manufacturer on a soil metabolism study indicates that P-100 was rapidly degraded under aerobic soil conditions at 22°C (64). The half-life at this temperature was approximately two hours and the parent material was not detected in soil extracts one day after treatment. The major soil metabolite of P-100 was PBC, a compound which is more persistent in the soil environment than P-100, but which is still rapidly degraded (half-life = 4.3 days). Further degradation of ^{14}C-PBC resulted in the formation of $^{14}CO_2$, with greater than 75% of the applied ^{14}C evolved as $^{14}CO_2$ 21 days after treatment.

Rapid degradation of P-100 to PBC was microbial dependent, but chemical processes may also contribute (64). In sterile soil, more than 90% of the applied P-100 remained four days after treatment. At 28 days after treatment, approximately half of the applied P-100 had degraded, primarily to PBC. P-100 degradation at 5°C was slower than at 22°C, but still relatively rapid (half-life = 0.586 days). PBC was again the main soil metabolite. Temperature had the greatest effect on the rate of PBC mineralisation; less than 10% of the applied ^{14}C was evolved as $^{14}CO_2$ 21 days after treatment.

A report on an NP-1 chemical spill compiled results of soil and water analyses at the spill site (42). Samples taken near a leaking holding dike did not contain detectable levels of IPBC (DL = 25 ppm). Expected levels of the chemical were 760 ppm, suggesting that the material had degraded within 28 days to less than 25 ppm. Final degradation products include carbon, nitrogen, chlorine, and iodine. IPBC was also not detected (DL = 10 ppm) in soils several days after being impacted by spills of 700 to 2000 ppm IPBC (11).

5.0 PHARMACOKINETICS

One pharmacokinetic study investigated plasma levels, extent of plasma protein binding, excretion, sites of retention and accumulation, and metabolic profiles of ^{14}C-IPBC in rats (36). Four groups of six rats (3 males, 3 females) received different dosages of ^{14}C-IPBC according to the following schedule:

Group A	single oral dose of 20 mg/kg
Group B	single intravenous dose of 0.5 mg/kg
Group C	7 daily oral doses of 20 mg/kg
Group D	single oral dose of 125 mg/kg

For oral administration, ^{14}C-IPBC was suspended in 0.5% carboxymethylcellulose. For intravenous administration, the compound was dissolved in ethanol:water (1:1 v/v). No adverse effects were observed following administration of either dose types. Pharmacokinetic results are summarized below.

5.1 Absorption, Transport, and Distribution

IPBC was quickly absorbed from the intestinal tract to the bloodstream, but was also rapidly eliminated. Levels of plasma radioactivity in Group D animals increased from 0.5 hours (17.4 ug equiv/ml) to 2 hours post dose (33.4 ug equiv/ml) at a similar rate to that observed in Group A. Control experiments demonstrated that IPBC did not bind extensively to plasma proteins (23-36% of parent dose). Peak plasma levels at 2 hours post dose showed similar values for protein binding (10.5-20%), indicating that the considerable metabolism of IPBC did not significantly affect the binding of ^{14}C to plasma protein.

Radioactivity was unevenly distributed in the tissues of Groups A and C. Group A levels in the liver and kidney declined steadily up to 240 hours, while levels in other tissues (e.g. skeletal muscle, lung, heart) declined more slowly. Fat tissue levels remained relatively constant (1.5-2.0 ug equiv/ml) from 12 to 240 hours post dose. In Group C, all tissue levels rapidly decreased from 3 hours to 12-14 hours post dose, assumed to mean after each daily dose. Although a number of tissues showed a steady decline in radioactivity up to 240 hours, some, especially fat, skeletal muscle, and skin, maintained approximately the same radioactivity concentrations from 96 to 240 hours.

5.2 Metabolism and Excretion

Blood sample analysis revealed that IPBC was rapidly metabolised, leaving little of the parent compound circulating in the plasma at 1 hour post dose. Thin layer chromatography analysis of plasma and urine revealed similar metabolic profiles. Plasma profiles indicated the presence of 3 to 4 metabolic peaks, while urine profiles showed 4 or 5 metabolites, including 2 or 3 'plasma-type' metabolites. These compounds were not identified.

The principal routes of IPBC excretion were the urine (32.3-50.9% of parent dose) and the lung (38.2-56.7% of parent dose), which is characteristic of mammalian metabolism of carbamate compounds (36). Small amounts were also eliminated in the feces or retained in the carcass.

5.3 Placental and Milk Transfer

No studies on placental or milk transfer of IPBC were located.

6.0 TOXICOLOGICAL EFFECTS

6.1 Mammalian Toxicity

The following toxicity tests used technical grade IPBC (97% pure). Toxicity ratings, as outlined in Appendix B, follow each oral and dermal toxicity value and reference.

			Toxicity
a) Acute Oral LD50:	Rat	1795 mg/kg (male) (15)	3
		1056 mg/kg (female) (15)	3
		1470 mg/kg(combined)(15)	3
b) Acute Dermal LD50:	Rabbit	>2000 mg/kg (16)	3
c) Primary Eye Irritation:	Rabbit	severe irritant (18)	
d) Primary Skin Irritation:	Rabbit	slight irritant (19)	
e) Sensitization:	Guinea Pig	non-sensitizer (20)	

			Toxicity
f) 4-Hour Inhalation LC50:	Rat	>6.89 mg/L (21)	3

In the above inhalation experiment, Sprague-Dawley rats exposed for 4 hours to 6.89 mg/L of IPBC in a 100 L chamber receiving an air flow of 16.7 L/min were observed for 14 days post exposure, then subjected to gross necropsy (21). Throughout the exposure period, all animals exhibited dyspnea, salivation, rhinorrhea, and lacrimation. Post exposure observations included bloody crusts on the nose, eyes, mouth, chest, and ears, rough coat, thin and languid wheezing, and urine stains. Gross observations of animals necropsied included dilatation and fluid-filling of renal pelvises, dark red pinpoint foci in the kidneys, and enlarged cervical lymph nodes. Necropsy of a female found dead at day 5 post-exposure showed unspecified findings in the spleen, intestines, stomach, lung, and nostrils.

g) Feeding Studies

Two short term toxicity studies on Sprague-Dawley rats have been cited in the literature (31). In a 13-week study, rats received 20, 50, or 125 mg IPBC/kg in corn oil five times per week. Animals treated at the highest dose exhibited transient behaviour alteration, decreased weight gain (males), increased absolute and relative liver weights, hepatocyte enlargement, and stomach lesions (males). Transient behaviour alteration and increased liver weights were also observed in both sexes at 50 mg/kg. The No Observed Effect Level (NOEL) was set at 20 mg/kg/day. Animals with a four-week recovery period did not show any treatment-related pathology, indicating reversibility of observed lesions. It was concluded that the test material and/or vehicle was a slight irritant to the rat.

In a second feeding study (31), rats were dosed with 60, 125, or 250 mg IPBC/kg/day (method unspecified) for four weeks. High dose animals exhibited decreased weight gain, food intake, and plasma cholinesterase (females only), and increased relative liver weights. Similar effects on weight gain, food intake, and liver weights were noted in the 125 mg/kg/day group. Animals receiving the lowest dose exhibited only a slight increase in relative liver weight. A NOEL was not established.

Two short-term range-finding studies for a multi-generation reproduction study were also cited (31). Mated female rats received 80 mg IPBC/kg/day by oral gavage, from day 0 to 20 of gestation. All animals were then sacrificed and examined. Although this study is of limited value due to lack of control data, overt toxicity at this dose was not observed. Male rats treated with 700 ppm (mg/kg unspecified) IPBC in the diet for 28 days also did not display overt toxicity.

6.2 Aquatic Toxicity

The following toxicity values are for technical grade (97% pure) IPBC. Conditions for each test are indicated by (s) - static bioassay, (f) - flow-through bioassay, or (u) - test conditions not indicated. Toxicity ratings for 96 hour tests follow each toxicity value and reference, according to the scale in Appendix C.

LC50:	Rainbow Trout		Toxicity
	24 hour	(f) >0.12 ppm (22)	
	48 hour	(f) 0.097 ppm (22)	
	72 hour	(f) 0.083 ppm (22)	
	96 hour	(f) 0.067 ppm (22)	5
		(u) 0.310 ppm* (30)	4
	NOEC - 96 hours**	(f) 0.049 ppm (22)	

* Toxicity value used to derive stormwater discharge criteria (Appendix D).

LC50:	Bluegill Sunfish		Toxicity
	24 hour	(f) >0.32 ppm (23)	
	48 hour	(f) 0.23 ppm (23)	
	72 hour	(f) 0.23 ppm (23)	
	96 hour	(f) 0.23 ppm (23)	4
		(u) 1.24 ppm (30)	3
		(u) 1.12 ppm (39)	3
	NOEC - 96 hours**	(f) 0.14 ppm (23)	

**NOEC = No Observed Effect Concentration

48 hr LC50:	Killifish	(u) 0.350 ppm (30)
	Daphnia magna	(s) 0.645 ppm (24)

A 21-day flow-through freshwater toxicity test using *Daphnia magna* has been completed (79). Chronic effects on first generation mortality, growth, and reproduction were evaluated and expressed as the maximum acceptable toxicant concentration (MATC), which lies between the no-observable-effect-concentration (NOEC), and the lowest-observable-effect-concentration (LOEC). Seven, 14, and 21-day EC50's (concentration of IPBC showing an effect on 50% of the population) were also calculated.

The 21-day geometric MATC was calculated to be 0.07 ppm, based on significant mortality, and reproductive and growth effects. The 21-day NOEC and LOEC were 0.05 ppm and 0.099 ppm, respectively. The 7-day, 14-day, and 21-day EC50's, based on mean measured IPBC concentrations, were 0.142 ppm, 0.136 ppm, and 0.133 ppm, respectively.

6.2.1 Bioconcentration

IPBC has been demonstrated to have a low potential for concentration in aquatic biota. A study in which Japanese carp (*Cyprinus carpio*) were exposed to IPBC concentrations of 0.5 to 5 ug/L in a flowthrough system found a bioconcentration factor of less than 4.5 (31).

6.3 Avian Toxicity

Results of toxicity testing on two bird species is listed below. The purity of IPBC used in the tests was 97% (75).

Acute Oral LD50:		
	Bobwhite quail	>3000 ppm (30)
		>7683 ppm (39)
	Mallard duck	>2900 ppm (30)
		>7182 ppm (39)

6.4 Comparative Toxicity

A comparison of several toxicity values of various antisapstain chemicals (Table 1) indicates that IPBC is highly toxic to fish, and is intermediate in toxicity of the chemicals available as alternatives to chlorophenates. However, because the chemical is used only in the antisapstain formulation NP-1 at a concentration of 7.6%, the relative risk of exposure should perhaps be examined in the context of the NP-1 product. Since only small amounts of IPBC would be released from the use of NP-1, risk to aquatic species would be decreased relative to using IPBC alone. Information listed in Table 1 also indicates that IPBC is one of the least orally and dermally toxic antisapstain compounds available.

7.0 CARCINOGENICITY

One long term study on the carcinogenic effects of IPBC on rats was located (27). Groups of 50 male and 50 female Sprague-Dawley rats were offered food *ad libitum* formulated with IPBC at dose levels of 20, 40, and 80 mg/kg/day for a period of 104 weeks. Blood counts were performed at weeks 53/54, 79, and 104 on control and high dose animals. Blood samples of 10 males and 10 females from each group were also taken in order to place in context results from earlier time points. A detailed necropsy was performed on all animals at time of sacrifice. Histopathologic examinations of organs were performed on all control and high dose animals, as well as on premature decedents from the low and intermediate dose groups.

There were no notable intergroup differences in water consumption, differential blood count, or mortality. A dose response reduction in body weight gain was seen in males of all dose groups. Females showed a moderate reduction in body weight gain in the intermediate dose group, and a marked reduction in the high dose group. High dose males also exhibited a slight reduction in food consumption.

Detailed necropsies showed no significant intergroup differences in organ weights, although all intermediate and high dose animals showed increased incidences of depressed and raised foci in the stomach, and of lesions in the keratinised stomach and submaxillary salivary glands. There was no evidence of carcinogenic potential in either sex. The NOEL in terms of major structural effects was set at 20 mg/kg/day for both sexes.

8.0 MUTAGENICITY

Three mutagenicity studies on IPBC have given negative results. One study measured the clastogenic potential of IPBC via micronuclei production in polychromatic erythrocytes of mice (25). A single dose of the chemical was administered by gavage to 4 groups of 15 male and 15 female mice at levels of 0,

200, 660, and 2000 mg/kg of body weight. Five males and five females from each group were sacrificed at 30, 48, and 72 hours after dosing. No statistically significant increase in micronuclei frequency was seen for any level tested, although toxic effects were observed at the higher dose levels. IPBC was thus concluded to be nonclastogenic at all levels tested.

Mutagenic activity was also tested by the *Salmonella typhimurium*/mammalian microsome mutagenicity test (26). Five concentrations of IPBC, equivalent to 500, 166.7, 55.6, 18.5, and 6.2 ug/plate, were evaluated in triplicate against five bacterial strains, TA1535, TA1537, TA1538, TA100, and TA98. Results showed that IPBC, with or without metabolic activation, did not induce a significant increase in the number of revertant colonies in any of the strains tested. Under these test conditions, IPBC was concluded to be nonmutagenic.

A test for the ability of IPBC to induce unscheduled DNA synthesis (UDS) in primary cultures of adult rat hepatocytes gave negative results (29). Liver cell cultures from young adult male F344 rats were treated with IPBC at concentrations of 3, 4.5, 6, 7.5, 9, 10.5, 12, and 13.5 ug/ml. Evidence of toxicity was noted in cells treated with the highest dose, but none of the cultures satisfied any of the evaluation criteria defining a positive response. It was therefore concluded that IPBC does not induce UDS in primary rat hepatocyte cultures when tested in dimethyl sulfoxide at concentrations which extend into the toxic range (29).

9.0 TERATOGENICITY AND REPRODUCTIVE EFFECTS

Several studies on reproductive and teratogenic effects of IPBC were located. In a preliminary oral toxicity study on mice (34), groups of eight sexually mature, mated female mice were dosed with 20, 50, or 125 mg/kg of chemical from day 6 to 15 *post coitum*. A control group of 8 mice received the vehicle (corn oil) over the same period of time. Animals receiving 20 and 50 mg/kg of the chemical did not show signs of maternal toxicity, embryotoxicity, or teratogenicity. Administration of 125 mg/kg, however, did elicit slight maternal toxicity in the form of reduced body weight gain from days 10 to 15 *post coitum*. No embryotoxic or teratogenic effects were noted. The NOEL was therefore set at 50 mg/kg/day for maternal toxicity, embryotoxicity, and teratogenicity.

In a subsequent large-scale oral teratogenicity study (33), groups of 35 mated female mice were administered 20, 50, or 125 mg of IPBC/kg from day 6 to 15 *post coitum*. A control group of 35 mice received vehicle only over the same period of time. The chemical did not elicit maternal toxicity, embryotoxicity, or teratogenicity in any dose group.

A similar study involved dosing groups of 28, 33, or 30 mated female Sprague-Dawley rats with 20, 50, or 125 mg IPBC/kg daily by oral gavage from day 6 through 15 of gestation (32). A control group of 38 rats received vehicle only over

the same period of time. No effects on clinical condition or on necropsy findings were noted between groups. Animals in the high dose group exhibited slight maternal toxicity in the form of reduced body weight gain from days 6 to 10 *post coitum*, but embryotoxic and teratogenic effects were not observed. Doses of 20 and 50 mg/kg also failed to elicit maternal toxicity, embryotoxicity, or teratogenic effects.

Another oral reproduction toxicity study (37) involved dietary administration of 0, 120, 300, and 750 ppm of IPBC (mg/kg unspecified) to groups of 25 male and female rats in each of two generations (parental, P and offspring, F1). After a 14 week pre-mating treatment period, parental animals in each generation were mated and the females allowed to rear their offspring to weaning.

Slight toxicity in the P males of the intermediate and high dose groups was observed, as indicated by reduced body weight gain and reduced food consumption during the pre-mating treatment period. Reduced body weight gain and food consumption were also seen in F1 males of the high dose group during pre-mating. There was no evidence of toxicity in either generation administered 120 ppm IPBC. Live birth index was slightly reduced in both generations at the highest dose, although post natal development of the offspring during the lactation period was not affected. The study concluded that IPBC at the doses tested had no effect on fertility or general reproductive performance in either generation.

10.0 IMPACTS OF OCCUPATIONAL EXPOSURE

No quantitative occupational exposure studies are available for IPBC (12). However, occupational studies using NP-1 (43-46) indicate that worker exposure potential to the chemical is minimal. Chemical exposure through inhalation may occur during maintenance or control work within the spray booth area, but such exposures would likely be for short periods of time only.

The extent of occupational hazard depends upon the concentration of NP-1 used, but the relative risks have not yet been evaluated (48). With a 1:45 dilution of NP-1, 71% of workers reported no physical symptoms, and approximately half stated that the odour was acceptable (48). Throat irritation or nausea were reported by 3% of respondents.

Because carbamate compounds other than IPBC can potentially inhibit blood acetylcholinesterase levels, concerns about blood chemistry impacts in workers using exposed to IPBC exist (47). Acetylcholinesterase inhibition results in accumulation of the neurotransmitter acetylcholine, with consequent overstimulation of nerves. Adverse effects may occur in the central nervous system, autonomic nervous system, and at neuromuscular junctions (57).

Studies on acetylcholinesterase inhibition in rats (71-73) have given negative results, indicating that IPBC is not a typical carbamate compound (12). A review of the chemical structure of the compound (48) supports the contention that IPBC does not inhibit the activity of blood cholinesterase.

In response to concerns about carbamate exposure, one company implemented an employee blood monitoring program which lasted two years. No changes in blood chemistry were detected over this period. In one instance, a mill employee was accidentally covered with NP-1 concentrate; blood tests conducted within two hours of exposure showed no change in blood chemistry.

BC Environment, Lands, and Parks has established an interim recommendation for an Acceptable Daily Intake (ADI) of IPBC by humans, based on intake by rats (66). The ADI is 2.80 mg/day for a 70 kg person; a derivation of this value is included in Appendix D.

11.0 ANALYTICAL METHODS OF DETECTION

Environment Canada has developed a method for measuring IPBC in effluents and sediments (35). Samples are extracted with methylene chloride and the extract is filtered and evaporated to dryness. The residue is dissolved in methanol and the sample is then analysed for IPBC by High Performance Liquid Chromatography (HPLC). The IPBC detection limit is 20 ug/L in effluents, and sediment detection limits are under evaluation.

An older method (9) from Koppers involves determination of iodine and chlorine in NP-1 samples by combustion in a Parr oxygen bomb. An alkaline hydrazine solution is used to convert any iodate present to iodide, and the solution is then titrated to determine total iodine and chlorine in the sample. Detection limits were not given.

The manufacturer also uses HPLC for analysis of IPBC in water samples (38). A standard calibration curve is prepared using IPBC in acetonitrile, and water samples are compared to the curve to estimate concentration of the chemical. The detection limit is 10 mg/L.

Recently, a new method for measuring IPBC levels on wood has been developed in Canada (40). The analytical technique is known as neutron activation analysis (NAA) and is based on the analysis of specific radiations emitted from iodine atoms in IPBC. Samples of treated wood are exposed to a low level source of radiation, and the resulting gamma ray emissions from the iodine are used to accurately measure its concentration down to 0.1 ppm. The technique is advantageous to mills because only small samples of wood are required, and extraction of IPBC from the wood is not required. Results are obtained quickly and are reproducible (41).

12.0 EXISTING LEGISLATION

British Columbia antisapstain legislation (14) stipulates that, effective September 1, 1990, concentrations of IPBC in effluents cannot legally exceed 120 ug/L, based on a derivation by Fox (60). A summary of his method is shown in Appendix E. Based on more recent data (22), a more stringent maximum level of 67 ug/L is proposed, but changes to the provincial antisapstain regulations are not planned at present.

Air quality regulations (14) prohibit emissions of greater than 7.0 mg of IPBC/second from chemical spray booth stacks. This value is based on the available technology for controlling spray booth emissions (17). A derivation of an interim emission standard is included in Appendix F (66).

13.0 CONCLUSION

Although the environmental behaviour of IPBC has not been completely documented, the work that has been done indicates that the chemical is degraded relatively quickly in soil, mainly through aerobic bacterial metabolism. Rapid hydrolysis occurs at pH 9, but not at pH 5. Soil adsorption has been shown to be moderate in several soil types. No leaching studies were located, but should be carried out considering that this is probably a major route of IPBC movement in the environment.

In mammals, IPBC is rapidly absorbed but also quickly metabolised and excreted. Its moderate oral and dermal toxicities (Table 1) make it of moderate concern to humans, but its potential for severe eye irritation should be noted. It has not been shown to be carcinogenic, mutagenic, or teratogenic. Effects of occupational exposure to IPBC have not been documented, although NP-1 exposure studies indicate that risk is minimal. Use of proper protective equipment and procedures is indicated.

The main concern associated with IPBC is its toxicity to aquatic life, especially fish. This fact warrants close regulation of IPBC releases to the environment and monitoring of environmental fate. Also of concern are the effects of long-term exposure of aquatic species. A reproductive study has been completed using *Daphnia magna*, but chronic toxicity studies on fish should also be done to determine an acceptable level of release of the chemical to the environment over time.

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Table 1: A comparison of toxicity values of antisapstain chemicals

	Oral LD50* Rat - mg/kg	Dermal LD50* Rabbit - mg/kg	Aquatic 96hrLC50* Fish species**-ppm
DDAC	84[55]	>1,600[55]	0.44[55] Bluegills 0.27[55]
IPBC	1,426[15]	>1,940[15]	0.065[22]
TCMTB	360[54]	324[54]	0.017[54] Chinooks 0.015[54]
Copper-8	702[55]	>1,960[55]	0.00016[55]
Sodium carbonate	4,000	not avail.	100
Sodium borate	2,660	>2,000	377
NaTCP	210[59]	270[59]	0.3-0.13[59]
NaPCP	71[60]	250[60]	0.048[61] Coho Salmon 0.032[53]
PCP	27[60]	39[60]	0.044[62] Bluegills 0.020[62]

*Values quoted are the lowest published for each species, and are based on 100% active ingredients, although less potent formulations may have been tested.

**Fish species is Rainbow trout unless otherwise noted.

APPENDIX A

Databases Searched for Information on IPBC

The following computerized databases were searched for information and publications on IPBC:

CA Search
Toxline
Toxlit
AQUIRE
Medline
RTECS
CCOHS

APPENDIX B

MAMMALIAN LETHAL TOXICITY CLASSES FOR CHEMICAL COMPOUNDS*

Toxicity Rating	Commonly Used Term	Oral/Dermal** (mg/kg)	Inhalation‡ (ppm-mg/L)
1	Practically Nontoxic	>15,000	>200
2	Slightly Toxic	5,000-15,000	20-200
3	Moderately Toxic	500-5,000	2-20
4	Very Toxic	50-500	0.2-2
5	Extremely Toxic	5-50	0.02-0.2
6	Ultra Toxic	<5	<0.02

*Toxicity ratings adapted from References 13, 69, and 74.

**Index: acute oral or dermal LD50.

‡Index: LC50 - four hour inhalation exposure.

APPENDIX C

AQUATIC LETHAL TOXICITY CLASSES FOR CHEMICAL COMPOUNDS*

Toxicity Rating	Commonly Used Term	Exposure Conc.** (ppm - mg/L)
1	Practically Nontoxic	>100
2	Slightly Toxic	10 to 100
3	Moderately Toxic	1 to 10
4	Very Toxic	0.1 to 1
5	Extremely Toxic	0.01 to 0.1
6	Ultra Toxic	<0.01

*Toxicity ratings adapted in consultation with reference 70.

**Index: 96 hour LC50 or EC50.

APPENDIX D

Calculation of an Acceptable Daily Intake (ADI) of IPBC for Humans

Following a method used by Fox (66), an ADI may be derived for humans based on the 20 mg/kg/day intake by rats in the 104 week carcinogenicity feeding study (27):

Calculation of human ADI based on rat NOEL

a) Safety factor used: 500x

i.e., - 100x for conversion of chronic animal to human data (interspecies variability)

- 5x for study quality uncertainty

b) Human IPBC ADI: = 20 mg/kg/day/500
= 0.04 mg/kg/day

c) For a 70 kg adult human: = 0.04 mg/kg/day x 70 kg
= 2.8 mg/day ADI

APPENDIX E

Derivation of Stormwater Effluent Criteria for IPBC

Following a method used by Fox (60), the formula for calculation of a stormwater discharge criteria is as follows:

Criteria = 96 hour LC50 x AF x EF x DMF x DF

where:
- AF = acute toxicity safety factor (1.0)
- EF = environmental fate safety factor (1.0)
- DMF = degradation product and metabolite hazards safety factor (1.0)
- DF = dilution factor (1.0)

The 96 hour LC50 used is the value for the most sensitive salmonid species, i.e. Rainbow trout. Fox used the value of 310 ppb for 40% IPBC (30), to give a value of 124 ppb total active ingredients. Antisapstain legislation limits effluent levels to 120 ppb (ug/L) (14).

N.B. Recently, a Rainbow trout 96 hour LC50 of 67 ppb was recorded (22). Using the above formula, a maximum concentration of 67 ppb (ug/L) of IPBC in stormwater would result.

APPENDIX F

Calculation of an Air Emission Guideline for IPBC

Based on the ADI given in Appendix D, an emission guideline is calculated below. A method used by Fox (66) is followed.

I. Assumptions

Adult
daily respiration = a) 20 m^3*
mean body weight = 70 kg
absorbs 100% of inhaled IPBC
respiration is only route of exposure

*This respiration value is based on values from the US Environmental Protection Agency (76).

II. Conversion of IPBC ADI to ug/m^3/day

Adult ADI_{70}

ADI = 2.8 mg/20 m^3/day
= 0.14 mg/m^3/day
= 140.0 ug/m^3/day (24 hour ambient air guideline)

III. Conversion of 24 hour ambient air guideline to 1 hour ambient air guideline

For use in subsequent dispersion modelling calculations, the 24 hour ambient air guideline should be converted to a 1 hour ambient air guideline. Using the formula (67):

$$C2 = C1 \times (T1/T2)^a$$

where C2 = 1 hour average concentration
C1 = concentration at time T1
T1 = time period of the original standard
T2 = 1 hour
a = exponent = 0.28

then the one hour ambient air guideline is as follows:

$$C2 = 140.0 \times (24/1)^{0.28}$$
$$= 340.9 \text{ ug/m}^3\text{/hour}$$

IV. Calculation of an Emission Guideline through Dispersion Modelling

Given meteorology data and stack characteristics, at an emission rate of 1 g IPBC/sec, maximum ground level concentration of IPBC will be 0.00019 g/m^3. For a maximum ground level concentration of 1 g/m^3 to arise, an emission rate of ~5000 g/sec would have to occur. For a maximum ground concentration of 341 ug/m^3 to arise, an emission rate of 1.71 g/sec would be required:

$$5000 \text{ g/sec} \times 3.41 \times 10^{-4} = 1.71 \text{ g/sec.}$$

Using an engineering safety factor of 35, as used to develop an emission guideline for chlorophenates (68), an appropriate guideline for IPBC is as follows:

$$1.71/35 = 4.9 \times 10^{-3} \text{ g/sec}$$
$$= 49 \text{ mg/sec}$$

N.B. Existing provincial legislation (14) allows spray booth emissions of 7.0 mg/second, based on capabilities of available technology.